

the specification.

The rejection is respectfully traversed.

Although there is no express support for the language objected to, it is well known to those skilled in the art that every ultrafiltration membrane has a molecular weight limit. Indeed, membranes are generally characterized as suitable or not suitable for a particular assay by their molecular weight limit. Moreover, those skilled in the art are well aware that nucleic acids with molecular weight limits below the limit of the membrane will pass through the membrane, and those with molecular weights higher than the limit of the membrane will not pass through the membrane. Nevertheless, in order to expedite allowance, claim 14 has been amended by deleting the term "predetermined" and substituting therefore the term "characterized". Those skilled in the art are well aware that every membrane is so characterized. Withdrawal of the rejection is respectfully requested.

The Examiner newly rejects claims 1-4, 9, 11, 14, 15, 17 and 19 under 35 U.S.C. §102(b) as being anticipated by Schneider, U.S. Patent No. 5,596,092. The Examiner states that Schneider discloses a process for the recovery/fractionation of nucleic acids contained in a liquid by dilution and ultrafiltration through a membrane to dryness.

By the accompanying amendment, claims 1, 6, 9 and 14 have been amended to recite that the process is for the fractionation by nucleic acid length, linear nucleic acid or contaminants in a liquid sample. Support for the amendment can be found in the paragraph bridging pages 4-5 of the specification, for example.

The present invention is directed to a process of fractionation based upon size, of solubilized linear nucleic acids contained in liquid samples. In contrast, Schneider relates to a precipitated complex of DNA; its solubility is used to purify. More specifically, a precipitate is created by complexing the DNA with a cationic detergent, an ionic exchange with NaCl is carried out, followed

by a washing to rid the sample of the salt. The solubility of the precipitated material is used to purify the same from proteinaceous contaminants. Thus Schneider is not a sized-based fractionation as is now expressly recited in the instant claims as amended.


Applicants further point out that the recitation at column 4, lines 50-52 of Schneider of an ultrafiltration step is a clear error. Firstly, the pore size of between 10 and 16 microns subsequently recited at line 52 (and also at column 3, lines 9-10) is much too large to be an ultrafiltration membrane. Furthermore, one skilled in the art would never carry out a precipitation-resuspension step using an ultrafiltration membrane; such a membrane has extremely small pores and would be unlikely to flow in the presence of the precipitate (*i.e.*, the precipitate would foul the membrane).

The Examiner also newly rejects claims 5-8, 12, 16 and 18 under 35 U.S.C. §103(a) as being unpatentable over Schneider in view of Simon, and claim 13 as being unpatentable over Schneider in view of Bussey. Simon is cited for its disclosure of the use of monvalent and bivalent cations in centrifugal ultrafiltration, and Bussey is cited for its disclosure that flow through an ultrafiltration membrane is pressure dependent and one could subject the samples to different pressures to obtain different flow rates of each species.

These claims are believed to be allowable by virtue of their dependence, for the reasons provided above.

Reconsideration, entry of the amendment, and allowance are respectfully requested in view of the foregoing.

Respectfully submitted,

  
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**Version With Markings to Show Changes Made**

1. (Twice amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample, comprising diluting said liquid sample, contacting the diluted sample with an ultrafiltration membrane to fractionate, and subjecting said diluted sample to a pressure differential to filter said diluted sample to dryness.
6. (Twice amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample, comprising providing an ultrafiltration membrane having an upstream and a downstream side, diluting said sample, and contacting said membrane with said liquid sample to fractionate said liquid sample, and subjecting said liquid sample to a pressure differential having a pressure less than 25 inches of Hg to filter said diluted sample to dryness.
9. (Twice amended) A process for the fractionation, by nucleic acid fragment length, of contaminants in a liquid sample, comprising increasing the concentration of said contaminants by adding to said sample a member selected from the group consisting of nucleic acid condensing agents and monovalent cations, and contacting the sample with an ultrafiltration membrane to fractionate, and subjecting said sample to a pressure differential.
- 13 (Twice amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample, comprising diluting said liquid sample, contacting the diluted sample with an ultrafiltration membrane to fractionate, and subjecting said diluted sample to a first pressure, followed by subjecting said diluted

Replacement Sheet

B1

1. (Twice amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample, comprising diluting said liquid sample, contacting the diluted sample with an ultrafiltration membrane to fractionate, and subjecting said diluted sample to a pressure differential to filter said diluted sample to dryness.

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6. (Twice amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample, comprising providing an ultrafiltration membrane having an upstream and a downstream side, diluting said sample, and contacting said membrane with said liquid sample to fractionate said liquid sample, and subjecting said liquid sample to a pressure differential having a pressure less than 25 inches of Hg to filter said diluted sample to dryness.

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9. (Twice amended) A process for the fractionation, by nucleic acid fragment length, of contaminants in a liquid sample, comprising increasing the concentration of said contaminants by adding to said sample a member selected from the group consisting of nucleic acid condensing agents and monovalent cations, and contacting the sample with an ultrafiltration membrane to fractionate, and subjecting said sample to a pressure differential.

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13 (Twice amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample, comprising diluting said liquid sample, contacting the diluted sample with an ultrafiltration membrane to fractionate, and

b4

subjecting said diluted sample to a first pressure, followed by subjecting said diluted sample to a second pressure different from said first pressure.

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14. (Amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample, comprising:

providing an ultrafiltration membrane having a characterized molecular weight limit;

providing said liquid sample wherein said linear nucleic acids comprise nucleic acids having a molecular weight below said characterized molecular weight limit of said membrane;

diluting said liquid sample; and

filtering said diluted sample with said ultrafiltration membrane to fractionate by subjecting said diluted sample to a pressure differential, whereby nucleic acids below said characterized molecular weight limit that absent said dilution would pass through said membrane are retained by said membrane.

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